Systematic review and meta-analysis: Does colonic mural thickening on computed tomography correlate with endoscopic findings at colonoscopy?

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Abstract

Background:

Colonic mural thickening (MT) is often reported on standard Computed Tomography (CT) examinations of the abdomen and pelvis. It often presents a dilemma for the clinician on whether any further evaluation is needed, especially in the absence of any set guidelines.

Objective:

To evaluate the significance of colonic mural thickening and to assess its correlation with colonoscopy.

Methods:

The search strategy was initially developed in MEDLINE and adapted for use in EMBASE, MEDLINE, NHS Evidence and TRIP. Studies were included if they'd reported colonic MT and subsequent colonoscopy in adults.

Results:

A total of 9 cohort studies examining 1252 patients were selected having undergone both CT and colonoscopy. Of the 1252 patients with MT, 950 had an abnormal colonoscopy. In the presence of MT, the pooled positive predictive value (PPV) of having any abnormal findings at colonoscopy was 0.73 (95% CI = 0.60 to 0.84). The pooled PPV for colorectal cancer, in the presence of MT reporting suspicion of cancer, was 0.63 (95% CI = 0.49 to 0.75) and MT suggestive of inflammation confirmed at colonoscopy was 0.97.

Conclusion:

The probability of having an abnormal colonoscopy in the presence of MT identified on CT is high, especially for inflammation. Asymptomatic cancers may also be detected, hence further endoscopic confirmation is reasonable when a finding of MT is demonstrated on CT examinations. Small sample sizes of the available studies and lack of data on the description of MT detected are the main limiting factors in this review.

Systematic review registration: PROSPERO CRD42016039378

1 INTRODUCTION

Computed Tomography (CT) scanning is a widely used imaging modality in the diagnostic workup of bowel pathologies. Recent advances in CT scanning, such as the multi-detector technology, allows higher accuracy and sensitivity in the diagnosis of abdominal pathologies[1]. One of the findings on abdomino-pelvic CT imaging is that of colonic mural thickening (MT). Colonic MT may be a reflection of inflammatory, infective, ischaemic and neoplastic pathologies[2]. On the other hand, MT may simply be due to benign strictures or collapsed segments of the colon.

In the setting of colonic MT, patients may have to undergo colonoscopy for further evaluation. However, currently there are no definitive guidelines as to when colonoscopic examination is needed. This often results in a diagnostic dilemma, especially when the clinical index of suspicion is low.

Several studies have evaluated the clinical significance of MT on CT imaging and its correlation with subsequent colonoscopic findings. Few studies have, however, illustrated the differentiating features of benign from malignant MT. In this study, we have conducted a systematic review of MT on abdominal CT imaging and its correlation with colonoscopic findings, to provide a more precise and reliable evidence for the clinical significance of MT identified on abdominal CT.

2 MATERIALS AND METHODS

The aim of this systematic review was to evaluate the significance of colonic MT on CT and its correlation with pathologies identified by colonoscopy performed within a four-week period. In accordance with the guidelines, our systematic review has been registered with the

International Prospective Register of Systematic Reviews (PROSPERO) and is reported according to the recommendations from the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) 2015 statement.

2.1 Study selection and eligibility criteria

We included studies which were (1) prospective and retrospective comparative cohort studies, case controlled studies, nested case-control studies and cross sectional studies (2) examined general adult human population of 18 years or older, both healthy subjects and those with colonic pathologies, (3) examined subjects who have had colonoscopic evaluation following a CT scan: Studies which described non-colonic MT i.e. sites other than from ileo-caecal valve to recto-sigmoid junction were excluded. (4) published in English and is available as full texts in the medical database between January 1980 and December 2015.

2.2 Search strategy

Literature search strategies were developed using medical subject headings (MeSH) and text words related to the title. The search was performed in Medline, EMBASE, NHS evidence and Trip using various combinations of keywords and subject headings for the articles related to the title. The search strategy was developed in MEDLINE (Ovid) using various refined search terms, to have as wider coverage as possible and was adapted to the syntax and subject headings of the other databases. The detailed digital search strategy is provided in a supplemental file. To ensure maximum capture, we had scanned the reference lists of included studies or the relevant reviews identified through the search for potential studies. The titles and abstracts of the selected studies were verified by two reviewers for ensuring relevance to the selected topic. Studies which did not fulfil the eligibility criteria were excluded. Those studies that fell between the borderlines were flagged up for further review.

Full text materials of all the relevant articles were reviewed by two independent reviewers using Scottish Intercollegiate Guideline Network (SIGN) checklist and a final selection was made.

2.3 Data Extraction and management

Data from the eligible studies were extracted using a standardized data extraction form. The following data were extracted: (1) study details (study year, study design, study aim); (2) study sample characteristics (sample size, inclusion/exclusion criteria, study mean age, gender distribution; (3) intervention (colonoscopic examination); (4) results (outcome of colonoscopy, site of abnormality, type of abnormality). Where necessary, further calculations were made from the available data. Data extraction was undertaken by two reviewers independently, to increase the accuracy and any subsequent disagreements were resolved by consensus or by involving a third reviewer.

2.4 Definitions

Colonic mural thickening was defined as thickening of >3mm in the presence of satisfactory distension. Right side colon was defined as from ileo-caecal valve to splenic flexure and the left side colon was defined as from splenic flexure to ano-rectal margin.

2.5 Risk of bias assessment

The risk of bias was assessed using SIGN checklists for methodology assessment. These considered study characteristics, sample characteristics, and statistical analysis and study outcomes. Each of these domains was assigned a score and the cumulative score over all domains determined the study quality (high, acceptable and poor). This was undertaken by one reviewer and double-checked by the other. Any disagreement was resolved by discussion.

2.6 Data synthesis and analysis

To perform statistical analysis, for each study, the number of colonic MT cases and the number of such cases that were subsequently confirmed to be abnormal (by colonoscopy) were extracted from the papers. Using these data, positive predictive value (PPV), defined as the proportion of MT cases that were confirmed abnormal by colonoscopy, and the corresponding 95% confidence intervals (CIs) for all studies were computed. A pooled PPV from all studies and their corresponding 95% CI were obtained by performing a random effects meta-analysis. Random effects meta-analysis was used because although it was reasonable to pool the results, the studies were expected to be heterogeneous. The PPVs for each study and the pooled PPV were summarised in a forest plot. Four subgroup analyses were performed based on various aspects; the cases where colonic MT was on the left side, the cases where colonic MT was on the right side, the cases where MT was suggestive of colorectal cancer and the cases where MT was suggestive of inflammation. All meta-analyses were performed in the R statistical program[3] using the function “metaprop” in package “meta”[4]. The “metaprop” function is specific to binary data, with 95% CIs calculated based on the binomial distribution.

3. RESULTS

Study characteristics of relevant studies

A total of 299 studies were retrieved of which 285 articles were excluded as inclusion criteria was not fulfilled. 4 articles were excluded, because they were only published as abstracts / conference abstracts. Of the remaining 10 full text articles, one article studied MT in both upper and lower gastrointestinal tract together, but no separate data were available for the colon. The selection process is summarised in figure 1. Rest of the 9 articles examining 1252

patients were selected for further analysis. The study characteristics are summarised in Table 1. The number of colonic MT cases (sample sizes) in the studies ranged from 27 to 505. The individual study PPVs ranged from 0.41 to 0.90 (Figure 2) and there was strong evidence for heterogeneity ($p<0.001$). The pooled PPV was 0.73 (95% CI = 0.60 to 0.84).

Table 1. Characteristics of studies included in the meta-analysis

Author, Year, Country	Colonoscopy findings	Gender (M/F)	Age (Mean)	Site of the Colon on CT
Al-khowaiter et al., 2014 (Canada)	NC 18	35/41	55	Not reported
	ANC 58			
Chowdhury et al., 2013 (USA)	NC 29	29/80	51	Not reported
	ANC 80			
Eskaros et al., 2009 (USA)	NC 10	88/62	Not reported	R/S 33
	ANC 22			L/S 89
Ince et al., 2014 (Turkey)	NC 50	290/215	49.15	Not reported
	ANC 455			
Nicholson et at., 2011 (United Kingdom)	NC 11	39/55	69.7	R/S 49
	ANC 83			L/S 30
Patel et al., 2009 (USA)	NC 55	32/62	54	R/S 34
	ANC 39			L/S 38
Rockey et al., 1995 (USA)	NC 10	Not reported	Not reported	Not reported
	ANC 22			
Troppmann et al., 2011 (Germany)	NC 5	35/27	60	R/S 11
	ANC 22			L/S 25
Uzzamann et al., 2012 (United Kingdom)	NC 70	Not reported	66.6	R/S 72
	ANC 95			L/S 93

MT at different sites of the colon

Only two studies (Uzzamann *et al.*, 2012 and Eskaros *et al.*, 2009); sample size 182, reported separate results for cases where colonic MT was on the left side. The results for the two studies were very similar (Figure 3), with no evidence of heterogeneity (p=0.694). The PPV was 0.64 (95% CI = 0.56 to 0.70). These two studies also reported cases where the abnormal MT was on the right side (Figure 4). The pooled PPV for the cases, where the MT on the right side, was 0.58 (95% CI = 0.43 to 0.72). The 95% CIs for the PPVs for the cases where MT was on the left and right sides overlapped so that, there was no evidence of difference in PPVs for the two groups.

MT and cancers

Two studies; sample size 51, reported separate results for colonic MT suggestive of cancers. The number of MT in the two studies was small and so the level of uncertainty was high (Figure 5). The pooled PPV was 0.63 (95% CI = 0.49 to 0.75).

MT and inflammation

Only two studies reported results for MT suggestive of inflammation on CT and subsequent endoscopy. The population size was very small; hence the level of uncertainty was again high (Figure 6). The pooled PPV was 0.97.

4. DISCUSSION

Although several studies have examined the significance of MT and its correlation with colonoscopy, this is the first systematic review and meta-analysis produced to date, based on standard CT examinations (not dedicated examinations such as CT Colonography). CT is widely used for the evaluation of the abdomen and pelvis in patients with abdominal

symptoms. CT is complementary to luminal examinations as it can help directly visualize the bowel wall, mesentery and surrounding peritoneal cavity. The thickness of the colonic wall on CT varies with luminal distension and as a result several different criteria have been used to assess MT[5-8].

MT is a hallmark of the underlying bowel abnormality and it is generally agreed that the diagnosis of abnormal MT should be elicited only in segments of adequately distended bowels in order to reduce a false positive diagnosis. Although MT may vary depending on the amount of bowel distension, the normal colonic wall should not exceed 3mm in thickness[9]. One study has graded the degree of MT as mild (3–6mm), moderate (6–12mm) and severe (>12mm)[10]. MT may be a result of neoplastic, inflammatory or ischaemic processes affecting the colon. Usually neoplastic conditions result in a more marked increase in MT as compared to benign causes. Focal thickening of the colon is also more indicative of a neoplastic lesion, whereas diffusive, long segment thickening is usually seen with benign causes (the exception being lymphoma, which can cause thickening of a long segment).

Several studies have evaluated the reported cases of MT on CT versus colonoscopy[10-14]. Rockey et al reported that the likelihood of detecting an abnormality on patients with MT was 67%[10]. Moraitis et al reported a positive correlation rate of 72%, Wolff et al reported that 73.9% of patients with MT had abnormalities on colonoscopy[11, 12]. Nicholson et al reported a PPV of 72% for CT[14]. This study, however, reported MT on both abdominopelvic CT (n=58) and CT colonography (n=36) (CTC) and concluded that CTC may have higher sensitivity and specificity compared to standard CT. Reported studies in scientific literature also recommend a colonoscopic examination following the diagnosis of MT on CT

examinations[13, 14, 15]. Uzzaman et al in a large study (n= 165) found that the correlation between MT and neoplastic lesion was 35.7% out of which 13.9% were of benign (polyps)[16].

In this meta-analysis, the number of cases with MT (sample sizes) in the studies ranged from 27 to 505. The pooled PPV of CT in patients with MT was 0.73 (95% CI = 0.60 to 0.84). It is difficult to make recommendations based on the PPV in the absence of "prevalence of abnormality" using colonoscopy, since a higher prevalence leads to higher PPV. Assuming the sensitivity and specificity obtained from Nicholson et al[14] (sensitivity 0.723, specificity 0.965), the relationship between the PPV and prevalence shows that the PPV of 0.73 corresponds to a prevalence of 11.5% (Figure 7). This suggests that the high pick up rate of CT scan for abnormalities is not due to the high prevalence.

This meta-analysis also showed that there was no difference between the left/right side in terms of pathology detection. Some studies had reported a higher sensitivity of CT scan in the detection of left sided MT as compared to the right[16-19]. The relatively higher mobility of the caecum makes it more likely to collapse and produce artefactual MT. There are also venous drainage pathways, hydrostatic pressures and collateral formation that could explain the different correlations between the right and left colonic segments.

The incidence of colorectal cancer in patients with MT on CT has been variable ranging from 14-27%[10, 11, 15, 16]. More importantly, many cancers were detected in asymptomatic patients. The rate of detected cancers in asymptomatic patients in these studies ranged between 16.6-80%. Therefore, the finding of MT on CT examinations may be the first sign of an underlying colonic cancer in asymptomatic individuals. There is a significant correlation between a CT finding of MT and a subsequent colonoscopic finding of neoplastic pathology. The association is particularly strong in cases of MT of the transverse colon[16]. The

association is also strong in white (Caucasian) patients and in those with a history of rectal bleeding[20]. Our findings showed, the pooled PPV from 2 small studies (sample size 51) was 0.63 (95% CI = 0.49 to 0.75). This should, however, be interpreted with care as the level of uncertainty was high.

There were several limitations in the reported studies. As only abnormal cases were further tested using gold standard, it was not possible to compute specificity and sensitivity since the normal cases were not tested using the gold standard. The sample size of the studies for subgroup analysis was small, hence the results should be interpreted with care. The finding of MT of the colon was not further elaborated in many of the studies such as degree of mural thickening, length of mural thickening, associated findings of lymphadenopathy, mesocolic stranding those could direct towards specific diagnoses. There were no data on the presence of mural thickening in the absence of adequate bowel distention. Furthermore, it was not clear from the studies whether the scans were reported by specialist GI radiologists or general radiologists. Future studies in this subject area should aim to address this gap by looking into these features and their association with colonoscopic findings in detail.

5. CONCLUSION

The findings of this meta-analysis suggest that patients with a finding of MT of the colon should, at the very least, be recalled and assessed fully because many of these patients may have significant colonic pathologies. The probability of having an abnormal colonoscopy in the presence of MT identified on CT is high especially for inflammation. Asymptomatic cancers may also be detected hence further endoscopic confirmation is reasonable when finding of MT is demonstrated on CT examinations. Small sample sizes of the available studies and lack of data on the description of MT detected are the main limiting factors in this review.

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Statement of interest:

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Competing interest:

None declared

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Figure Legends:

Figure 1: Flow chart demonstrating study selection process based on inclusion criteria.

Figure 2: Forest plot for all cases and abnormalities.

Figure 3: Forest plot for the cases where abnormal colonic thickening is on the left side.

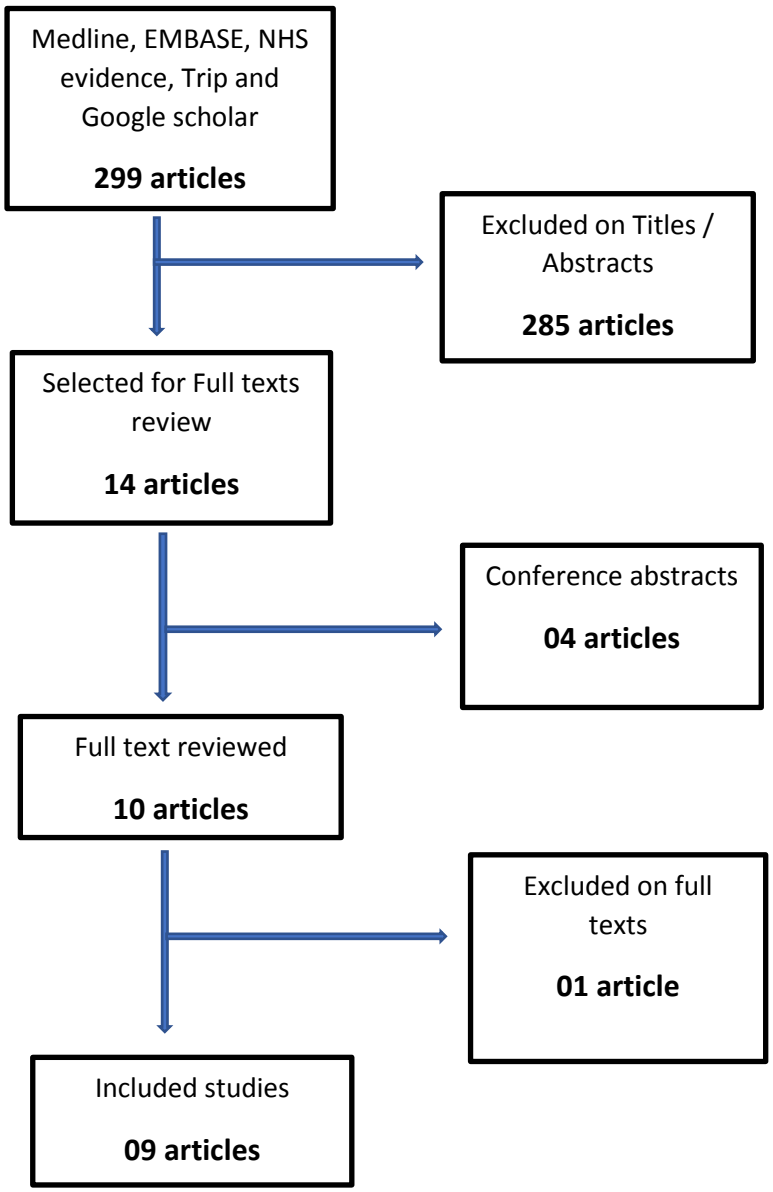
Figure 4: Forest plot for the cases where abnormal colonic thickening is on the right side.

Figure 5: Forest plot for abnormal mural thickening cases suspected to be cancers

Figure 6: Forest plot for cases where CT identified MT suggestive of inflammation

Figure 7: Relationship between prevalence and PPV from assuming the sensitivities obtained from Nicholson et al. (Sensitivity =0.723, specificity =0.965)

Figure 1. Flow chart demonstrating study selection process based on inclusion criteria



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	ANC 39			L/S 38
Rockey et al., 1995 (USA)	NC 10	Not reported	Not reported	Not reported
	ANC 22			
Troppmann et al., 2011 (Germany)	NC 5	35/27	60	R/S 11
	ANC 22			L/S 25
Uzzamann et al., 2012 (United Kingdom)	NC 70	Not reported	66.6	R/S 72
	ANC 95			L/S 93

(R/S, Right side colon; L/S, Left side colon; NC, Normal colonoscopy; ANC, abnormal colonoscopy)

Figure 2. Forest plot for all cases and abnormalities

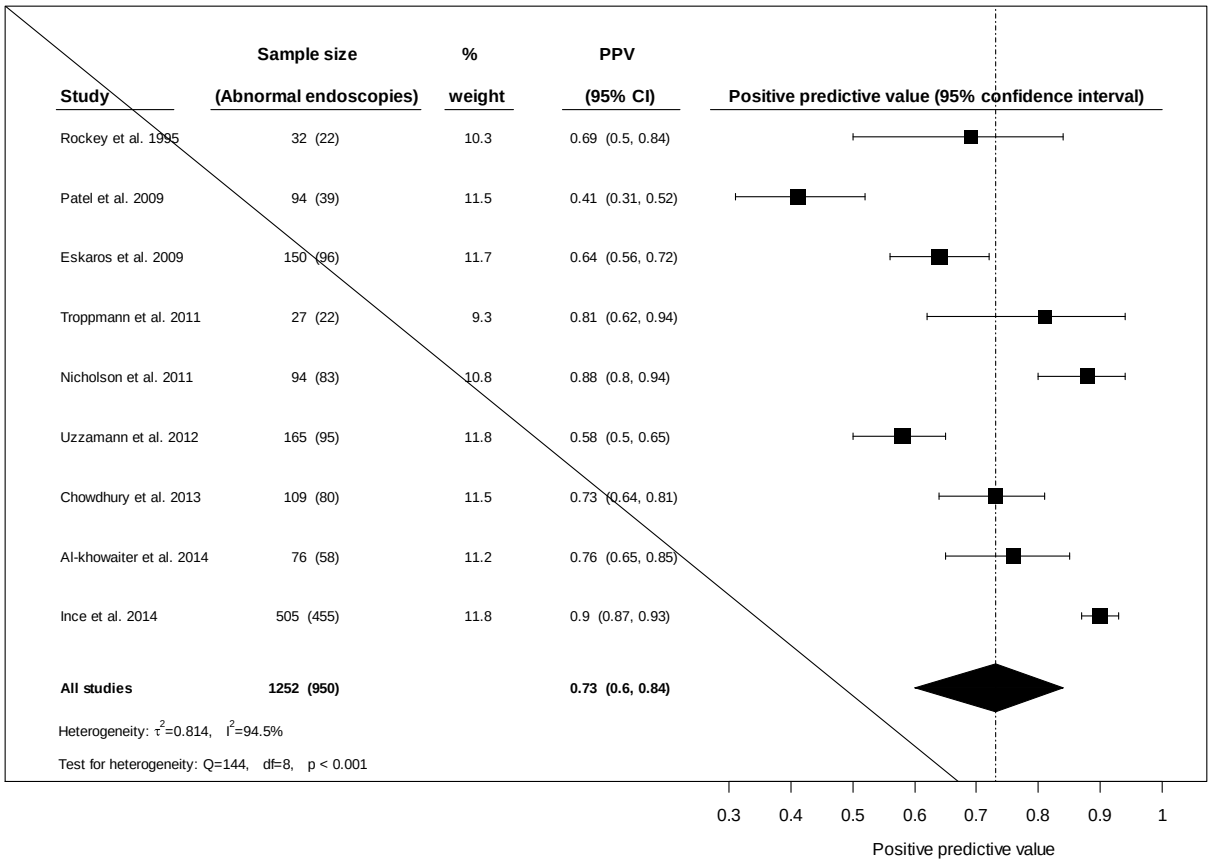


Figure 3. Forest plot for the cases where abnormal colonic thickening is on the left side

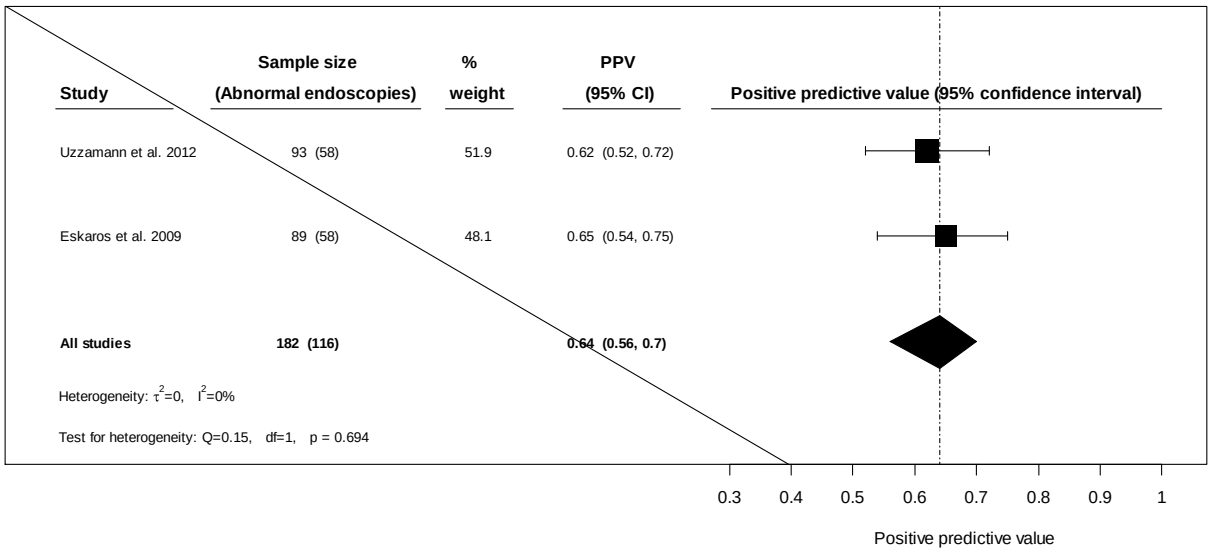


Figure 4. Forest plot for the cases where abnormal colonic thickening is on the right side

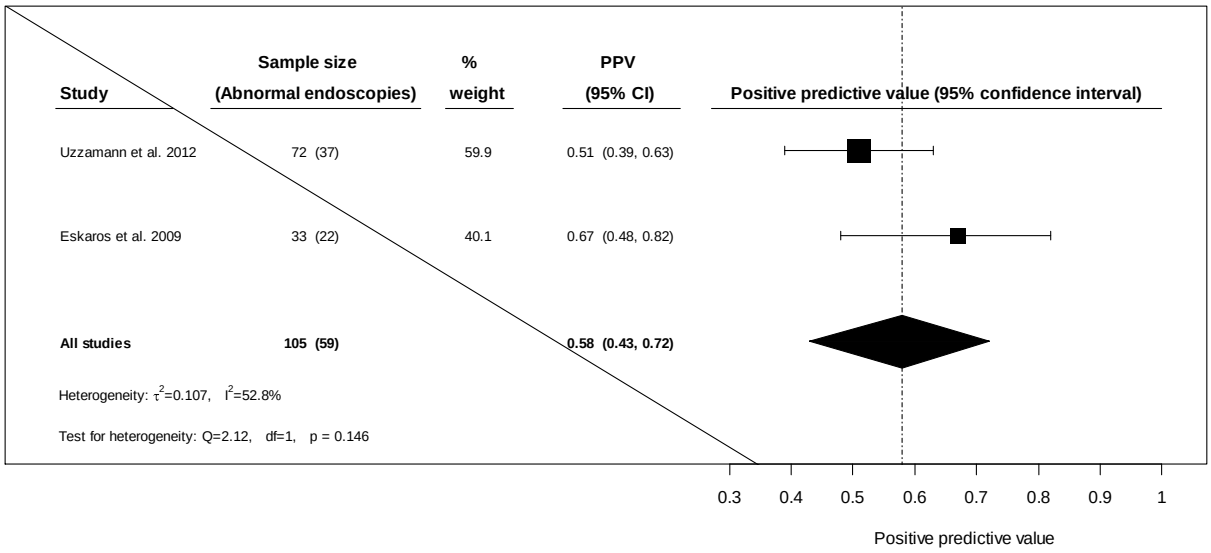


Figure 5. Forest plot for abnormal mural thickening cases suspected to be cancers

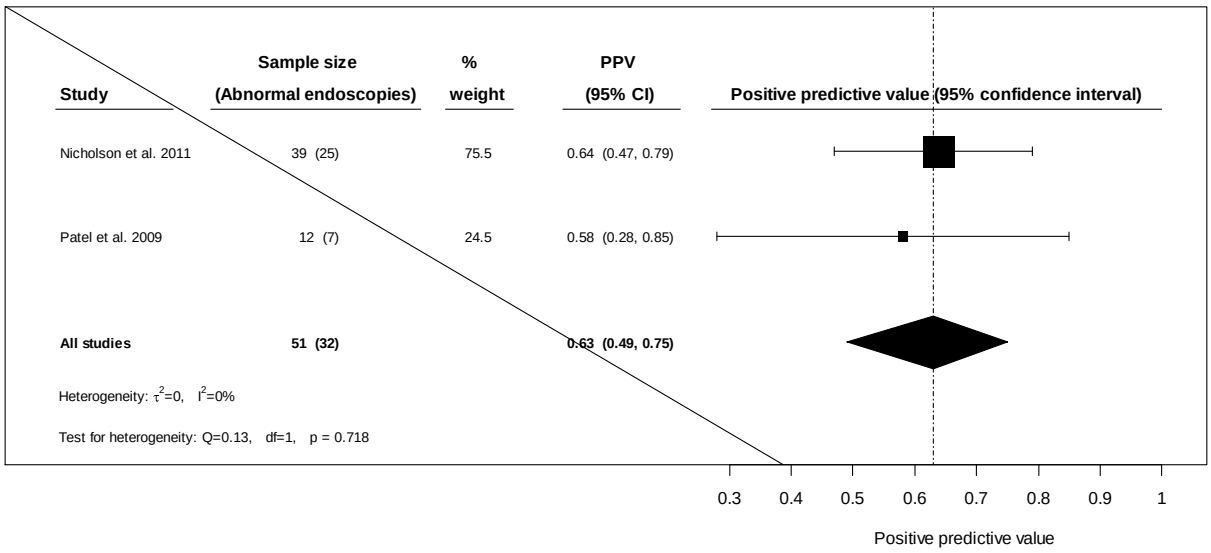


Figure 6. Forest plot for cases where CT identified MT suggestive of inflammation

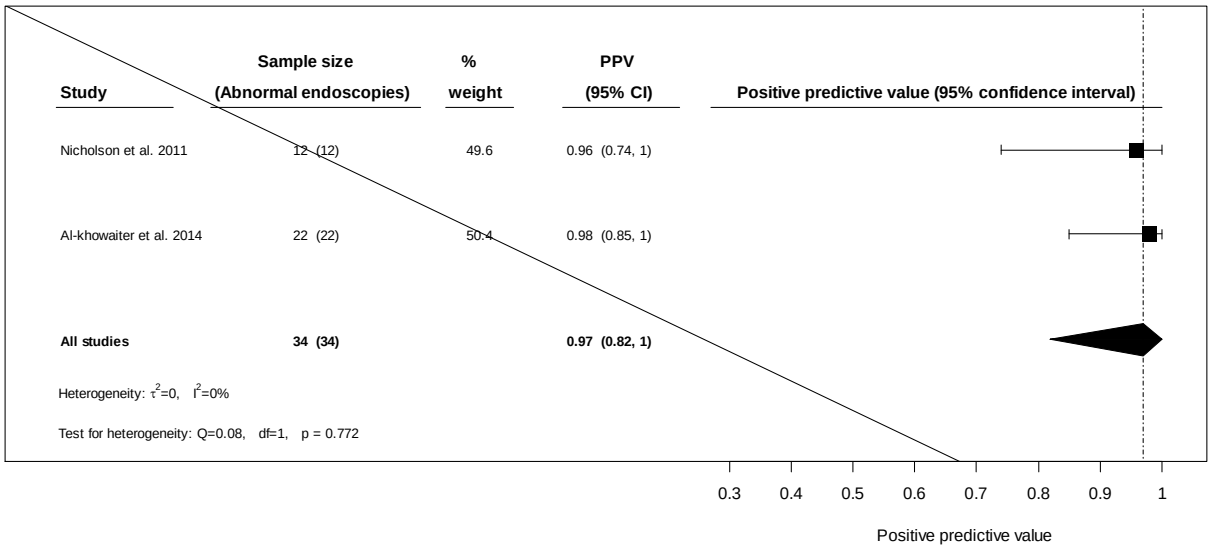
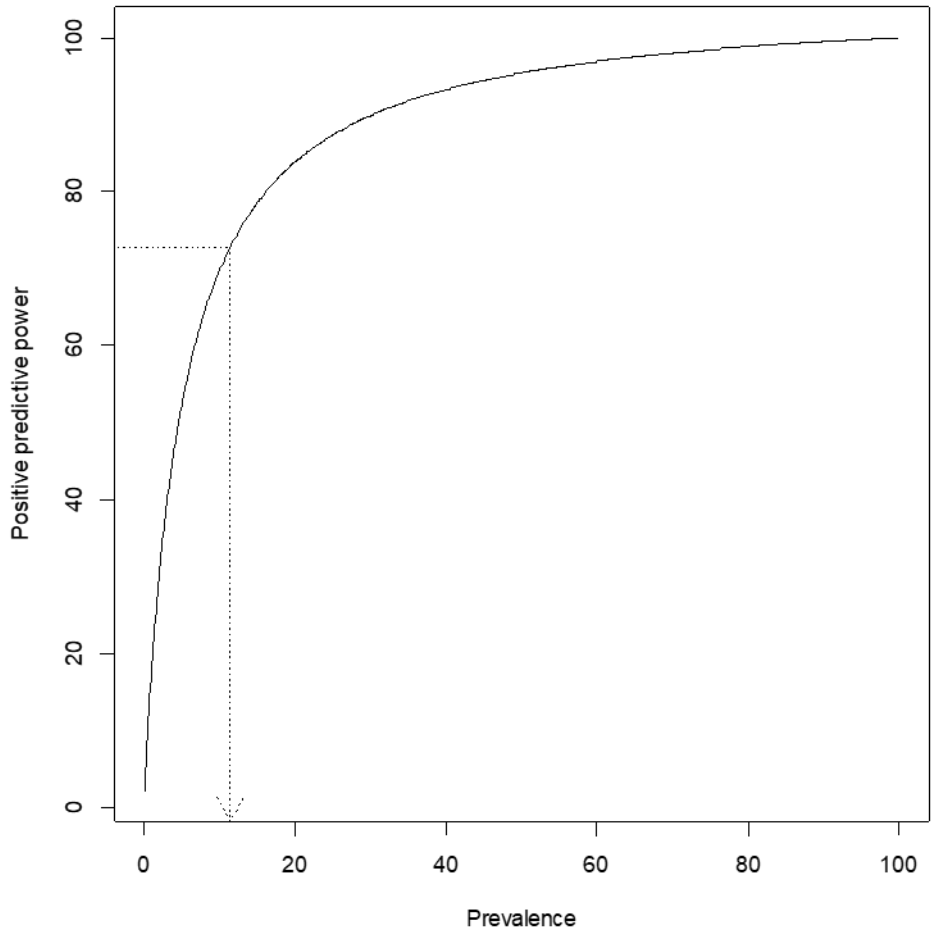


Figure 7. Relationship between prevalence and PPV from assuming the sensitivities obtained from Nicholson et al. (Sensitivity =0.723, specificity =0.965)


Positive predictive power
0
20
40
60
80
100
Prevalence
0
20
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